# (19) World Intellectual Property Organization International Bureau





## (43) International Publication Date 29 March 2001 (29.03.2001)

#### PCT

# (10) International Publication Number WO 01/21154 A3

- (51) International Patent Classification7: A61K 9/14, 9/107
- (21) International Application Number: PCT/US00/25880
- (22) International Filing Date:

21 September 2000 (21.09.2000)

(25) Filing Language:

English

(26) Publication Language:

English

- (30) Priority Data: 60/154,964 21 September 1999 (21.09.1999) U
- (71) Applicant: RTP PHARMA INC. [US/US]; 4364 South Alston Avenue, Durham, NC 27713-2280 (US).
- (72) Inventors: PACE, Gary, W.; 6913 Hunters Way, Raleigh, NC 27615 (US). MISHRA, Awadhesh, K.; Apartment 201, 670 de Gaspe, Nuns Island, Verdun, Quebec H3E 1HB (CA). SNOW, Robert, A.; 118 Cratin Lane, West Chester, PA 19380 (US).
- (74) Agent: CRAWFORD, Arthur, R.; Nixon & Vanderhye P.C., Suite 800, 1100 North Glebe Road, Arlington, VA 22201-4714 (US).

- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- (88) Date of publication of the international search report: 25 October 2001

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

1154 A3

(54) Title: SURFACE MODIFIED PARTICULATE COMPOSITIONS OF BIOLOGICALLY ACTIVE SUBSTANCES

national Application No

PCT/US 00/25880 A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K9/14 A61K A61K9/107 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 A61K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Category ° Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. 2,3,5. X WO 99 29300 A (MISHRA AWADHESH K ; PARIKH INDU (CA); MOUSSA ISKANDAR (CA); RTP PHA) 8-14 17 June 1999 (1999-06-17) the whole document WO 99 29316 A (MISHRA AWADHESH K ; MOUSSA X 2,3,5, ISKANDAR (CA); CLARKE NUALA M (IE); CYCL) 8-14 17 June 1999 (1999-06-17) the whole document US 5 827 822 A (FLOC H ROBERT ET AL) X 2.8 - 1427 October 1998 (1998-10-27) the whole document Further documents are listed in the continuation of box C. Patent family members are listed in annex. Χİ Special categories of cited documents: "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "A" document defining the general state of the art which is not considered to be of particular relevance \*E\* earlier document but published on or after the international 'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another clation or other special reason (as specified) 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-\*O\* document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled \*P\* document published prior to the international filing date but later than the priority date claimed \*&\* document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 16 March 2001 26/03/2001 Name and mailing address of the ISA Authorized officer

Form PCT/ISA/210 (second sheet) (July 1992)

2

European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016

Marttin, E

PCT/US 00/25880

| ation) DOCUMENTS CONSIDERED TO BE RELEVANT  |   |
|---|---|
| Citation of document, with indication, where appropriate, of the relevant passages  | Relevant to claim No.   |
| US 5 091 187 A (HAYNES DUNCAN H) 25 February 1992 (1992-02-25) cited in the application column 7, line 48 -column 8, line 44 column 9, line 50 -column 10, line 19 column 11, line 14 -column 12, line 61 column 16, line 60 -column 17, line 48; claims; examples 5,6; tables 2,3                    | 1,3-6,<br>8-14  |
| US 5 560 931 A (EICKHOFF W MARK ET AL)<br>1 October 1996 (1996-10-01)   | 1,3-6,8,<br>9,11,13,<br>14  |
| the whole document  |   |
| US 4 801 455 A (LIST PAUL H ET AL) 31 January 1989 (1989-01-31) the whole document  | 1,3-6,8,<br>9,13,14   |
| GB 1 527 638 A (BAYER AG)<br>4 October 1978 (1978-10-04)<br>the whole document  | 1,3,4,6,<br>8,9,14  |
| WO 00 40219 A (DEXCEL LTD ; DOMB ABRAHAM J (IL)) 13 July 2000 (2000-07-13) the whole document   | 2,3,8-14  |
| US 6 057 289 A (MULYE NIRMAL) 2 May 2000 (2000-05-02) cited in the application the whole document   | 2-5,8-14  |
| WO 99 49848 A (RTP PHARMA INC)<br>7 October 1999 (1999-10-07)<br>the whole document   | 2-5,8-14  |
| WO 00 10531 A (RTP PHARMA INC) 2 March 2000 (2000-03-02) the whole document   | 2-5,8,9,<br>13,14   |
| WO 00 41682 A (LG CHEMICAL LIMITED ; KIM MYUNG JIN (KR); KIM SUN JIN (KR); KWON KY) 20 July 2000 (2000-07-20) cited in the application page 5, line 10 - line 21 page 6, line 1 - line 19 page 7, line 16 - line 31 page 8, line 10 -page 10, line 16 claims 1-3,5-7,11-15,17-20; example 20; table 2 | 1,3-5,<br>8-14  |
|   | US 5 091 187 A (HAYNES DUNCAN H) 25 February 1992 (1992-02-25) cited in the application column 7, line 48 -column 8, line 44 column 9, line 50 -column 10, line 19 column 11, line 14 -column 12, line 61 column 16, line 60 -column 17, line 48; claims; examples 5,6; tables 2,3  US 5 560 931 A (EICKHOFF W MARK ET AL) 1 October 1996 (1996-10-01)  the whole document  US 4 801 455 A (LIST PAUL H ET AL) 31 January 1989 (1989-01-31) the whole document  GB 1 527 638 A (BAYER AG) 4 October 1978 (1978-10-04) the whole document  WO 00 40219 A (DEXCEL LTD ;DOMB ABRAHAM J (IL)) 13 July 2000 (2000-07-13) the whole document  US 6 057 289 A (MULYE NIRMAL) 2 May 2000 (2000-05-02) cited in the application the whole document  WO 99 49848 A (RTP PHARMA INC) 7 October 1999 (1999-10-07) the whole document  WO 99 49848 A (RTP PHARMA INC) 2 March 2000 (2000-03-02) the whole document  WO 00 10531 A (RTP PHARMA INC) 2 March 2000 (2000-03-02) the whole document  WO 00 41682 A (LG CHEMICAL LIMITED ;KIM MYUNG JIN (KR); KIM SUN JIN (KR); KWON KY) 20 July 2000 (2000-07-20) cited in the application page 5, line 10 - line 21 page 6, line 1 - line 19 page 7, line 16 - line 31 page 8, line 10 - page 10, line 16 claims 1-3,5-7,11-15,17-20; example 20; |

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-15 relate to an extremely large number of possible compositions, non-aqueous media, surfactant systems and hydrophilic substances. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compositions, non-aqueous media, surfactant systems and hydrophilic substances claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compositions prepared in the examples, and to the non-aqueous media, surfactant systems and hydrophilic substances disclosed in the examples on pages 22-28, and to the general concepts of "non-aqueous media", "surfactant systems" and "hydrophilic substances".

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

anomation on patent ramily members

national Application No PCT/US 00/25880

| Patent document cited in search report | . – | Publication date | -        | Patent family member(s) | Publication date         |
|--|-----|------------------|----------|-------------------------|--------------------------|
| · ·                                    |     | <u> </u>         |          |                         | <u> </u>                 |
| WO 9929300                             | A   | 17-06-1999       | AU       | 1809499 A               | 28-06-1999               |
|  |     |                  | AU       | 1817499 A               | 28-06-1999               |
|  |     |                  | EP       | 1039893 A               | 04-10-2000               |
|  |     |                  | NO       | 20002991 A              | 09-08-2000               |
|  |     |                  | WO       | 9929316 A               | 17-06-1999               |
| WO 9929316                             | Α   | 17-06-1999       | AU       | 1809499 A               | 28-06-1999               |
|  |     |                  | AU       | 1817499 A               | 28-06-1999               |
|  |     |                  | EP       | 1039893 A               | 04-10-2000               |
|  |     |                  | NO       | 20002991 A              | 09-08-2000               |
|  |     |                  | WO       | 9929300 A               | 17-06-1999               |
| US 5827822                             | Α   | 27-10-1998       | AU       | 2219097 A               | 17-10-1997               |
|  |     |                  | AU       | 709548 B                | 02-09-1999               |
|  |     |                  | ΑU       | 6644196 A               | 1 <b>9-</b> 03-1997      |
|  |     |                  | BG       | 62875 B                 | 31-10-2000               |
|  |     |                  | BG       | 101443 A                | 31-03-1998               |
|  |     |                  | BR       | 9606603 A               | 30-09-1997               |
|  |     |                  | CA       | 2202887 A               | 06-03-1997               |
|  |     |                  | CN       | 1164828 A               | 12-11-1997               |
|  |     |                  | CZ       | 9701248 A               | 17-09-1997               |
|  |     |                  | DE       | 789561 T                | 10-06-1999               |
|  |     |                  | EP       | 0789561 A               | 20-08-1997               |
|  |     |                  | ES       | 2129381 T               | 16-06-1999               |
|  |     |                  | HU       | 9801052 A               | 28-09-1998               |
|  |     |                  | JP       | 3009742 B               | 14-02-2000               |
|  |     |                  | JP       | 10509462 T              | 14-09-1998               |
|  |     |                  | NO       | 971890 A                | 24-04-1997               |
|  |     |                  | PL       | 319898 A                | 01-09-1997               |
|  |     |                  | SI       | 9620014 A               | 30-04-1998               |
|  |     |                  | SK       | 53697 A                 | 08-10-1997               |
|  |     | •                | WO       | 9707787 A               | 06-03-1997               |
|  |     |                  | WO       | 9735603 A               | 02-10-1997               |
| US 5091187                             | Α   | 25-02-1992       | US       | 5091188 A               | 25-02-1992               |
|  |     |                  | AT       | 181234 T                | 15-07-1999               |
|  |     |                  | AU       | 7852891 A               | 11-11-1991               |
|  |     |                  | CA       | 2078990 A               | 27-10-1991               |
|  |     |                  | DE       | 69131349 D              | 22-07-1999               |
|  |     |                  | DE       | 69131349 T              | 18-11-1999               |
|  |     |                  | DK       | 533690 T                | 22-11-1999               |
|  |     |                  | EP       | 0533690 A               | 31-03-1993               |
|  |     |                  | ES       | 2134776 T               | 16-10-1999               |
|  |     |                  | GR       | 3030825 T               | 30-11-1999               |
|  |     |                  | IN       | 173056 A                | 05-02-1994               |
|  |     |                  | KR       | 159114 B                | 01-12-1998               |
|  |     |                  | MX       | 25532 A                 | 01-10-1993               |
|  |     |                  | RU       | 2100030 C               | 27-12-1997               |
|  |     |                  | WO       | 9116068 A               | 31-10-1991               |
|  |     |                  | US       | RE35338 E               | 24-09-1996               |
|  |     |                  | US       | 5246707 A               | 21-09-1993               |
|  |     |                  | ZA       | 9103122 A               | 29-04-1992               |
| US 5560931                             | Α   | 01-10-1996       | AT       | 198148 T                | 15-01-2001               |
|  |     | •                | AU       | 4862796 A               | 27-08-1996               |
|  |     |                  | CA       | 2207304 A               | 15-08-1996               |
|  |     |                  |          |                         |                          |
|  |     |                  | DE<br>Ep | 69611287 D<br>0808154 A | 25-01-2001<br>26-11-1997 |

Information on patent family members

national Application No
PCT/US 00/25880

| Patent document cited in search repor | t        | Publication date       |          | Patent family member(s) | Publication date                        |
|---------------------------------------|----------|------------------------|----------|-------------------------|---|
| US 5560931                            | Α        |                        | JP       | 10513200 T              | 15-12-1998                              |
|                                       |          |                        | WO       | 9624332 A               | 15-08-1996                              |
| US 4801455                            | Α        | 31-01-1989             | DE       | 3623376 A               | 21-01-1988                              |
|                                       |          |                        | AT       | 61730 T                 | 15-04-1991                              |
|                                       |          |                        | AU       | 597688 B                | 07-06-1990                              |
|                                       |          |                        | AU       | 7553687 A               | 14-01-1988                              |
|                                       |          |                        | CA       | 1302257 A               | 02-06-1992                              |
|                                       |          |                        | DE       | 3768734 D               | 25-04-1991                              |
|                                       |          |                        | DK       | 359787 A                | 12-01-1988                              |
|                                       |          |                        | EP       | 0256285 A               | 24-02-1988                              |
|                                       |          |                        | ES       | 2039214 T               | 16-09-1993                              |
|                                       |          |                        | FI       | 873044 A                | 12-01-1988                              |
| •                                     |          |                        | GR       | 3001710 T               | 23-11-1992                              |
|                                       |          |                        | JP<br>PT | 63023811 A<br>85292 A,B | 01-02-1988<br>01-08-1987                |
|                                       |          |                        | ZA       | 8705044 A               | 24-02-1988                              |
|                                       |          |                        |          |                         | 24-02-1900                              |
| GB 1527638                            | Α        | 04-10-1978             | DE       | 2557615 A               | 23-06-1977                              |
|                                       |          |                        | AU       | 503449 B                | 06-09-1979                              |
|                                       |          |                        | AU       | 2073676 A               | 29-06-1978                              |
|                                       |          |                        | FR       | 2335204 A               | 15-07-1977                              |
|                                       |          |                        | NL       | 7614155 A               | 22-06-1977                              |
|                                       |          |                        | NZ       | 182909 A                | 20-09-1978                              |
|                                       |          |                        | ZA       | 7607506 A               | 30-11-1977                              |
| WO 0040219                            | Α        | 13-07-2000             | AU       | 1796200 A               | 24-07-2000                              |
| US 6057289                            | Α        | 02-05-2000             | AU       | 4681200 A               | 17-11-2000                              |
|                                       |          |                        | WO       | 0066140 A               | 09-11-2000                              |
| WO 9949848                            | <b>А</b> | 07-10-1999             | AU       | 3377099 A               | 18-10-1999                              |
| NO 3343040                            |          | 07 10 1555             | EP       | 1067908 A               | 17-01-2001                              |
|                                       |          |                        | SE.      | 0003449 A               | 23-11-2000                              |
|                                       |          |                        |          |                         |   |
| WO 0010531                            | A        | 02-03-2000             | AU       | 5570599 A               | 14-03-2000                              |
| WO 0041682                            | Α        | 20-07-2000             | AU       | 3080500 A               | 01-08-2000                              |
| NO UUTIUUL                            | •        | · · · <del>_</del> · · | BR       | 0004152 A               | 21-11-2000                              |
|                                       |          |                        | OK.      | 0004132 A               | 7 T T 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 |